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Interstitial granulomatous drug reaction following intravenous ganciclovir

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No conflict of interest.

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Letter to the Editor

Dear Sir

Interstitial granulomatous dermatitis (IGD) is a distinct inflammatory reaction pattern of the skin. Differential diagnoses for this histological pattern span from interstitial granuloma annulare (IGA), interstitial granulomatous drug reaction, IGD of connective tissue diseases in particular arthritis, leukemia cutis, necrobiosis lipoidica, granulomatous mycosis fungoides, deep fungal infections to paraneoplastic diseases. Interstitial granulomatous drug reaction (IGDR) is recognized as a drug-induced interstitial granulomatous inflammatory reaction pattern. Clinically, most cases of IGDR have been described as erythematous to violaceous plaques on the extremities or intertriginous areas of the skin. Calcium-channel blockers, angiotensin-converting enzyme inhibitors, beta-blockers, lipid-lowering agents, antihistamines, anticonvulsants, sennoside, antidepressants, furosemide and herbal medications have been described as eliciting drugs for IGDR (1,2, 4, 5, 6).

We here report a case of IGDR following intravenous application of ganciclovir.

Case Report

A 57-year-old woman presented with slightly erythematous, sharply demarcated and exquisitely tender subcutaneous nodules of 5 mm diameter on the palms of both hands and the circumference of the soles of her feet (Fig.1).

Her past medical history included a renal transplantation in 1984 for chronic glomerulonephritis, past CMV pneumonitis, latent tuberculosis, chronic hepatitis C, sick-sinus-syndrome, spinal claudication and immunoglobulin deficiency of the common variable type.

In January 2007 the patient was hospitalized for fever of unknown cause.

Intravenous ganciclovir (Cymevene®) was started on January 29th 2007 for a CMV-pneumonia. No other new medication was introduced until the patient noticed the appearance of slightly erythematous sharply demarcated and exquisitely tender nodules of 5 mm diameter on the palms of both hands and the circumference of the soles of her feet (Fig.1) at the end of February 2007.

The patient presented for a dermatological assessment. The clinical differential diagnosis spanned from atypical erythema exsudativum multiforme without epidermal involvement triggered by a drug or a viral infection to piezogenic papules or neutrophilic eccrine hidradenitis. A punch biopsy of the lesion was performed, revealing a dense, diffuse inflammatory infiltrate throughout the reticular dermis (Fig.2(a)) composed of histiocytes and some eosinophilic granulocytes distributed interstitially and focally in a palisaded array around small, discrete bundles of sclerotic collagen (Fig. 2(b)). Superficial and deep perivascular infiltrates of lymphocytes were observed (Fig. 2(a), (b)).

The histological differential diagnosis included interstitial granulomatous dermatitis and other granulomatous skin disorders such as the interstitial form of granuloma annulare. Given the rapid appearance of multiple erythematous sharply demarcated and painful nodules in an annular pattern, the strict temporal association of ganciclovir therapy with onset of lesions, the histology as well as the rapid and complete spontaneous resolution within 2 weeks after cessation of the putatively causative drug (no other new drug was administered before the onset of lesions), the diagnosis of interstitial granulomatous drug reaction was retained.

Discussion

Interstitial granulomatous dermatitis is defined by a histological inflammatory pattern observed in several conditions including interstitial granuloma anulare, interstitial granulomatous dermatitis with arthritis with linear cords on the trunk or proximal extremities, interstitial granulomatous dermatitis with plaques, interstitial granulomatous dermatitis associated with infection such as borreliosis or induced by drugs. Granulomatous dermatitis as consequence of drug therapy presents clinically as erythema nodosum-like lesions or a disseminated maculopapular eruption on the one hand. On the other hand, red to violaceous plaques on the axillary folds and groin (6) and erythematous sharply demarcated and painful nodules in an annular pattern are reported in interstitial granulomatous drug reaction. These lesions show perivascular lymphohistiocytic infiltrates, degeneration and fragmentation of elastic and partly collagen fibers with intense basophilic staining, some lymphocyte invasion of the vascular wall and extravasation of erythrocytes with interstitial mucin deposits on histology (1, 3). The clinical differential diagnosis of such infiltrated plaques includes T-cell lymphoma, erythema anulare centrifugum, granuloma anulare and subacute cutaneous lupus erythematosus.

Reported agents eliciting an interstitial and granulomatous drug reaction are calcium-channel blockers, angiotensin converting-enzyme inhibitors, beta-blockers, lipid-lowering agents, antihistamines, anticonvulsants, furosemide, sennoside, antidepressants and herbal medications, but no relationship to ganciclovir has been reported to date. In our case, clinical presentation, chronological association with ganciclovir use and cessation and the histological picture speak in favor of IGDR. Based on our case report, we suggest to broaden the spectrum of causative drugs

and to include antiviral therapy with ganciclovir as a potential trigger for interstitial granulomatous dermatitis.

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Figure legends

Fig. 1

Right palm showing slightly erythematous, sharply demarcated, well palpable and exquisitely tender subcutaneous nodules of 5 mm diameter (circles indicate lesions). Similar lesions were observed on the other palm as well as on the lateral aspects of both feet.

Fig. 2

Low-power magnification of hematoxylin-eosin stain with superficial and deep interstitial and granulomatous inflammatory infiltrate of the biopsy on right hand and high-power magnification (insert) of the specimen taken from the right hand showing degeneration and fragmentation of elastic and partly collagen fibers with intense basophilic staining, some lymphocyte invasion of the vascular wall and extravasation of erythrocytes.

Fig.1

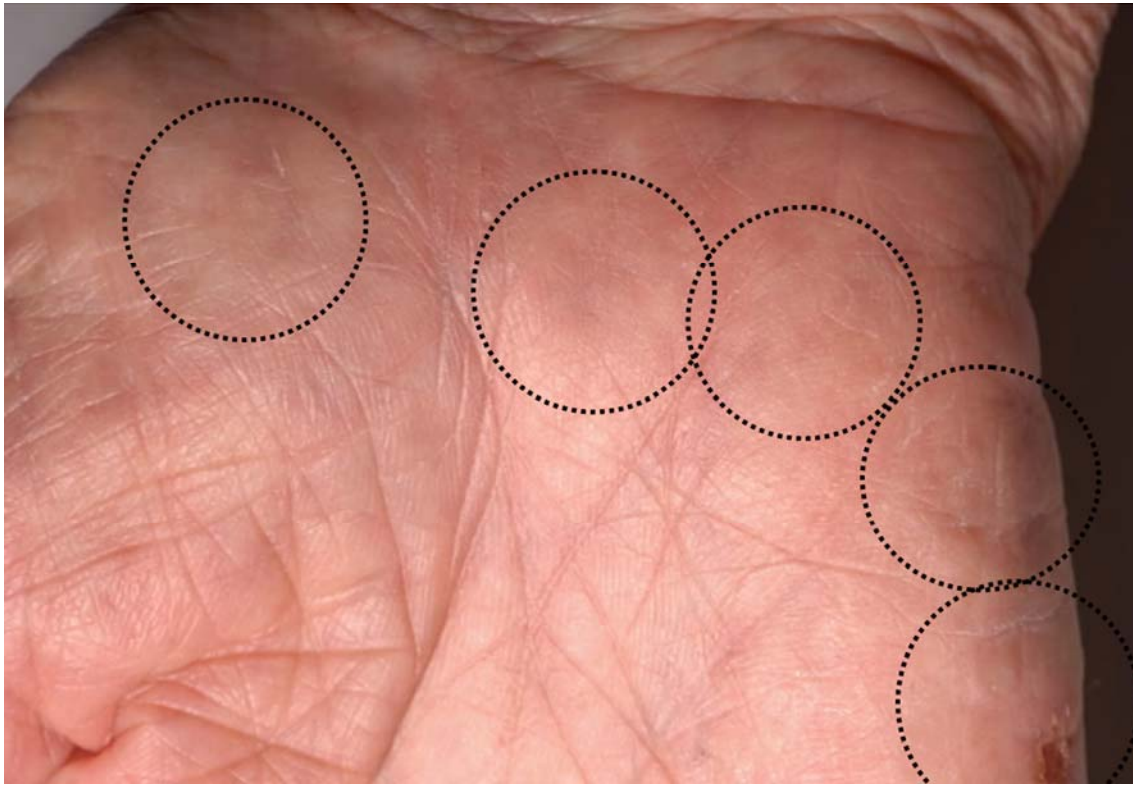


Fig.2

